

FIG. 1

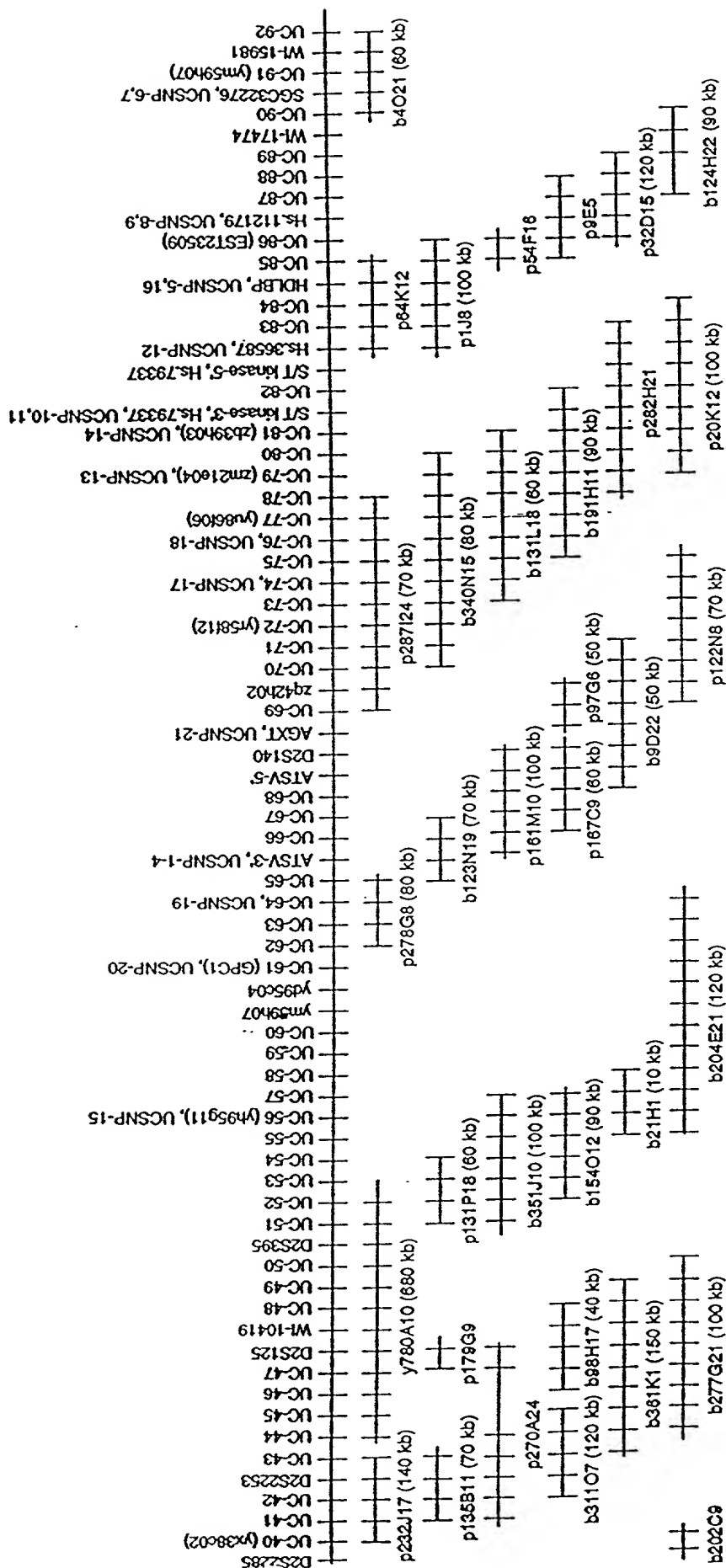


FIG. 2

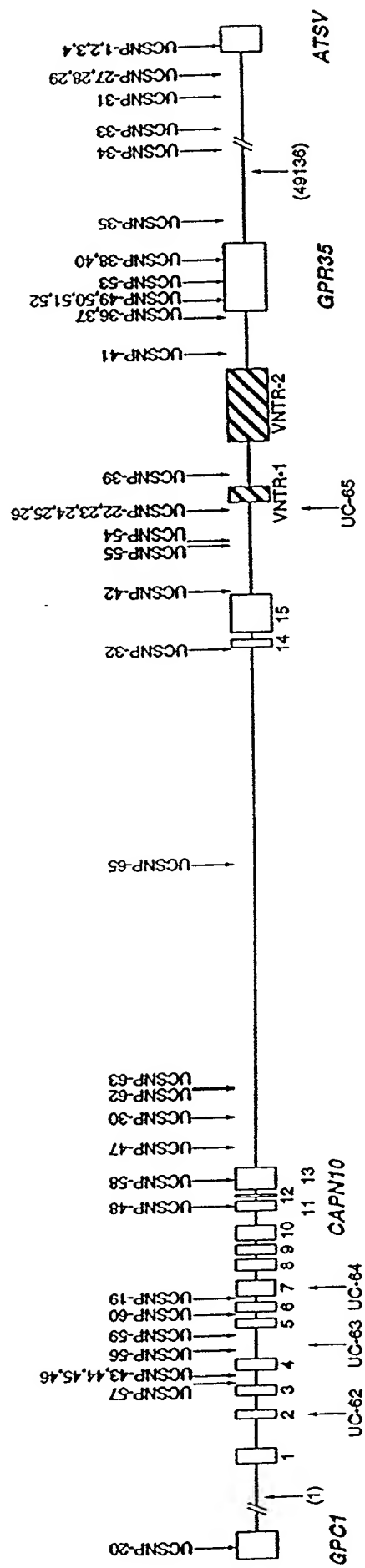


FIG. 3

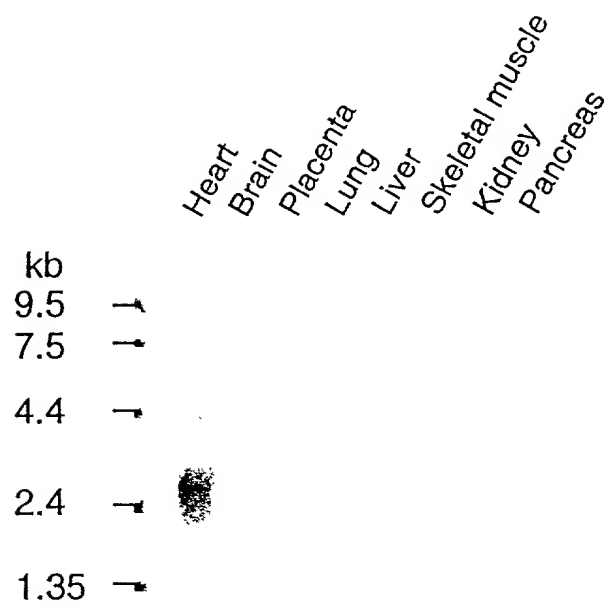


FIG. 4

		Domain I	Domain II	
hCAPN5	-----MFSCVKPYEDQMSALRQDCRRRKVLFDPLFPATDDSLYY-KGTGPG-----AVRWKRPKGCIEDPRFLVDG	67		
hCAPN6	-----MGPPPLKLFKNQKYELQKQCKKGRLEFCDPTFLPENSLEFFNRLLG-----KVWVKRPQDLSDDPHLLVGN	67		
hCAPN3	MPTVISASVAPRTAAEPRSGPVHPAQSATEAGGNGSGIYSAISRNFPIIGVKEKTFEQLHKCKLEKVLVDPEFPDDETSLFYSQKFP-----IQFVWKRPEICENPRFIIDG	115		
hCAPN9	MPYLY-----RAPGPQAHVP-----KDARITHSSSQSFEQMRQECLEQRTLFEDADFPASNSSLFYSERPQ-----IPFVWKRPGELIKVKNPEFLGG	83		
hCAPN1	-----MSEEIITPVYCTGVSQAQVQKQARELGLG-----RHENAIIKYLQDQYDQLRVRLCQSGTLFRDEAFPPVQSLGYKDLGPNSSKTYGKWKRPTELLSNPQFIVDG	101		
hCAPN2	-----HAGIAAKLAKDREAEGLG-----SHERAIKYLQDYALRNECLEAGTLFQDPSFPAIPSAFGKELGYPSSKTRGHRWRKRPTEICADPQFIIG	91		
hCAPN8	-----HAALAGVSKQRAVAEGLG-----SNQNAVLYKLGQDFETLRRKQCLNSGVLFKDPFEFPACPSALGYKDLGPGSPDTQGIWVKRPTELCNPPQFIVG	91		
hCAPN10	----------MRARGATPARELFRDAFPAADSSLECDLSTPLAQFREDITWRRPQETCATPRLEPDD	59		
hCAPN5	ISSHDLHQGGQVGNWFAVACSSSLASRESLWQKVIIPDKWEQEWDPKACAYAGIFHFHFWRLG-HYDVVIDERLPTVNNQLIYCHSNSRNEFWCALVEKAYAKLAGCYQALDGGNTADALV	186		
hCAPN6	ISNHQLIQGLRGNKAMISAFSCSLAVQESHWTIKAI PNHKDQEWDPKPEYAGIFHFHFWRLG-HYDVVIDERLPTVNNQLIYCHSNSRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	187		
hCAPN3	ANRTDICQGGELGDCWFLAAIACITLNQHLLFRVIP-----HDQSFENYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	229		
hCAPN9	ATRTDICQGGELGDCWFLAAIACITLNQHLLFRVIP-----QDQSEFGPYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	197		
hCAPN1	ATRTDICQGGALGDCWFLAAIACITLNQHLLFRVIP-----HQSFQENYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	215		
hCAPN2	ATRTDICQGGALGDCWFLAAIACITLNQHLLFRVIP-----LQSFQENYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	205		
hCAPN8	ATRTDIRQGGGDCWFLAAIACITLNQHLLFRVIP-----RDQSFQKDYAGIFHFQFWRYGEWVDVDDCLPTVNNQLVFTKSNHRNEFWCALVEKAYAKLAGCYQALDGLTITTDIIM	205		
hCAPN10	PRGQVQKGLGDCWFLCAACALQKSRHLLDQVIP-----PGQSWADQEYRGSTFCRIWQFGRWVEVTTDDRLPCLAGRLCFSRQREDVFWLPLEKVIKVGHSYELHMAQGVADALV	175		
hCAPN5	DFTGGVSEPIDLTEGDFANDETKRNQLFERMLKVHSGGLISASIKAV-----TAADK-----EARLACGLVKGHAYAVTDV	258		
hCAPN6	DFTGTLAEIIDMQGRITDVEEYKLGLELYTFTKGLICCSIESP-----SQEEQ-----EVETDGLKGYTYTMDI	259		
hCAPN3	DFTGGVAEFTQKE-----APSDMYKIMKKAIERGSLMGCSIDGNTMTYGTSPGLNHGELLARHVRNMDNSLQDSLDLPRGSDERPTIIPVQYETRMAGCLVGRHAYSVTGL	341		
hCAPN9	DFTGGVAEFTQKE-----APENFYEILEKALKRGSLLGCFIDT-----RSAES-----EARTPFGLKGHAYSVTGI	261		
hCAPN1	DFTGGVTEWELRK-----APSDLYQIILKALERGSLGCSIDIS-----VLDK-----EATTFKLVKGHAYSVTGA	279		
hCAPN2	DFTGGIAEWELKK-----PPNLFKIIQKALQKGSLLGCSIDIT-----S-----AADS-----EATTFKLVKGHAYSVTGA	269		
hCAPN8	DFTGGISEFYDLKK-----PPENLYYIIQKALKRGSLLGCSIDVS-----T-----AAEA-----EATTFKLVKGHAYSVTGV	269		
hCAPN10	DLTGGLAERWNLKGVAGSGGQDRPGRWEHRTCRQLLHLADQCLISCC-----VLS-----PRAGARELGEFHAIVSDI	245		
hCAPN5	RKVLRLGHLLAFFKSEKLDMLRLNPNWGEREWGMPWSDTSEEQKVSSEKREKMGVTQDDGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	373		
hCAPN6	RKRLRGERLVEVFSTEKLYMVLRLNPLGRQEWGMPWSEISEEQQVITVDRMLGLVMSDDGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	371		
hCAPN3	DEVFP-----KGEVKVLRLNPNWQVWNGSWSDRWQWSDVFDKDEKARLQHQTVEDGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	444		
hCAPN9	DQVSF-----RGQRIELIRIRNPWQVWNGSWSDSPEWRVSGPAEQKRLCHTALDDGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	364		
hCAPN1	KQVNY-----RGQVVSILIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	381		
hCAPN2	EEVES-----NGSLQKILIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	371		
hCAPN8	EEVNF-----HGRPEKILIRNPNWGEVWNTGAWSDSSSEWNNVDPYERDQLRVKME-DGEFWMTEFEDVCRYPTDIIKCRVINTSHL-SIHKTWEEARL-----HGAWTLHEDPRQNRG	371		
hCAPN10	RELQ-----QAGQCILLRIQNPWGRRCWQGLWREGGEGNSQVDAVAASELLSQLQ-EGEFWVEEEFREFDELTVGYPTVEAGHLQSLYTERLLCHTRALPGAWVKG-----QSA	352		
hCAPN5	GGCINHKDTFFQNPQYIFEVKKPED-----EVLICIQRRPKSTRREGKGENLAIGFDIYKVE-----E-----NRQYRMHSL-----QHKAASSIYNSRVSFLRTDQPEGRVYIPT	472		
hCAPN6	GGCYNRRDTFLQNPQYIFTEDEGH-----KVHLSQKQDLRTYRRMGPRDNYIIGFELFKVE-----M-----NRFRHLHLYIYERAGTSTYIDTRTVFLSKYLKKGSYVLNPT	472		
hCAPN3	GGCRNFPDTFWTNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ASLFTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYIMHREVSQRFLRPPSEYIVVPS	559		
hCAPN9	GGCRNFLTFTWNPQYRLKLEEDD-----DPPDSEV-ICSFVLALMQRNRKDRKLG-ANVLTIGFAIYEVPEKMHGK-CHLQKDFFLYNASKARSKTYIMHREVSQRFLRPPSEYIVVPS	471		
hCAPN1	GGCRNYPATEFWNPQYRLKLEEDD-----DEEDGES-GCTFLVGLIQKRRRRQRKMG-EDMHTIGFGIYEVPEELSGQTNIHLKSNFFLNRRARERSDTFINLREVLNRFKLPPEGYILVPS	499		
hCAPN2	GGCRNYPNTFWNPQYRLKLEEDD-----DEEDGES-GCTFLVGLIQKRRRRQRKMG-EDMHTIGFGIYEVPEELSGQTNIHLKSNFFLNRRARERSDTFINLREVLNRFKLPPEGYILVPS	487		
hCAPN8	GGCLNYPGTWYNPQYRLKLEEDD-----DEEDGES-GCTFLVGLIQKRRRRQRKMG-EDMHTIGFGIYEVPEELSGQTNIHLKSNFFLNRRARERSDTFINLREVLNRFKLPPEGYILVPS	489		
hCAPN10	GGCLNYPGTWYNPQYRLKLEEDD-----DEEDGES-GCTFLVGLIQKRRRRQRKMG-EDMHTIGFGIYEVPEELSGQTNIHLKSNFFLNRRARERSDTFINLREVLNRFKLPPEGYILVPS	471		
hCAPN5	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----530			
hCAPN6	MFQHGRTSEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN3	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN9	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN1	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN2	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN8	TFEPHGTGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN10	TFELKADGEFLRLVFTDVPNSCRELRLEDEPPHT-----C-----WSSLCGYPQLVTQVHVILGAAGLKD-----532			
hCAPN5	-----SPTGANSYVIIKCEGDKVRSAVQKG-----TSTPEYNVKGIFRYKKLSQPIITQVQVNR-----VLKDFELGQVHLKADPDCRDLKSLYLRKKGKPT	618		
hCAPN6	-----ANETVNPYLIKOGKEEVRSVPQKN-----TVHAIPTQAIYFRTTIDIPIIQVQVNR-----KFCDFLQGVTLADPDCRDLKSLYLRKKGKPT	620		
hCAPN3	VVNKKDLKTHGFTLESRSMLALMDTGGSKLNLQEFHILWNIKAWKIFKHYYDQSGTINSYEMRANVNDAGFHLANNQLYDITMYADKHMNDIFDSFICCFVRLBGFRAFHAF	799		
hCAPN9	VLQKKDKIKFKKLSLISCKNIISLMDTSGNGKLEFDEFKVFWDKLGQWNLFLRFDADKSGTMYELRTALKAAQFQLSSHLQLVILRYADEELQDFDDFLACLVLRLNARSVQAL	668		
hCAPN1	IISKHKDLRTKGFSLSCRSVNLNADRDNGLKGLVEFNILNIRNYLSIFRKFDLKSQSHSAYEMRMAIESAGFKLAKKLYELIITRYSEPDLAVDFDNFVCLVRLTETLFRFFKTL	692		
hCAPN2	VLAKRQDIKSDGFSIETCKIMVMDLSDGSGKLGKEFYILWTKIQYQKIYREIDVDRSGTINSYEMRMAIESAGFKLAKKLYELIITRYSEPDLAVDFDNFVCLVRLTETLFRFFKTL	679		
hCAPN8	VLAKRQDIKSDGFSIETCKIMVMDLSDGSGKLGKEFYILWTKIQYQKIYREIDVDRSGTINSYEMRMAIESAGFKLAKKLYELIITRYSEPDLAVDFDNFVCLVRLTETLFRFFKTL	682		
hCAPN10	-----PCFPFSVPEGPGPRCVRITLHQHCRPSD-----TEFHPIGHFIFQVPEGGRSQDAPPLLQEPILLSCVPHRYAQEVSRCLLPLAGTYKVVVSTYLPDTBGAFTVTIATRIDRPSIHSQ	654		
hCAPN5	PSNLPGTVAVHILSSTSLMAV-----639			
hCAPN6	AKVKQGHISFKVISSDDLT-----641			
hCAPN3	DKDQGGIILNVLKWLQTHYA-----821			
hCAPN9	STKNKEFIHLNINEFIHLTMNI-----690			
hCAPN1	DTDLGQVVTDFLKKLQTLTFA-----714			
hCAPN2	DPENTGTIELDLISWLCFSVL-----700			
hCAPN8	DKDQNGIVQLSLAEWLCCVLV-----703			
hCAPN10	EMLGQFLQEVSVMAVMKT-----672			

FIG. 5

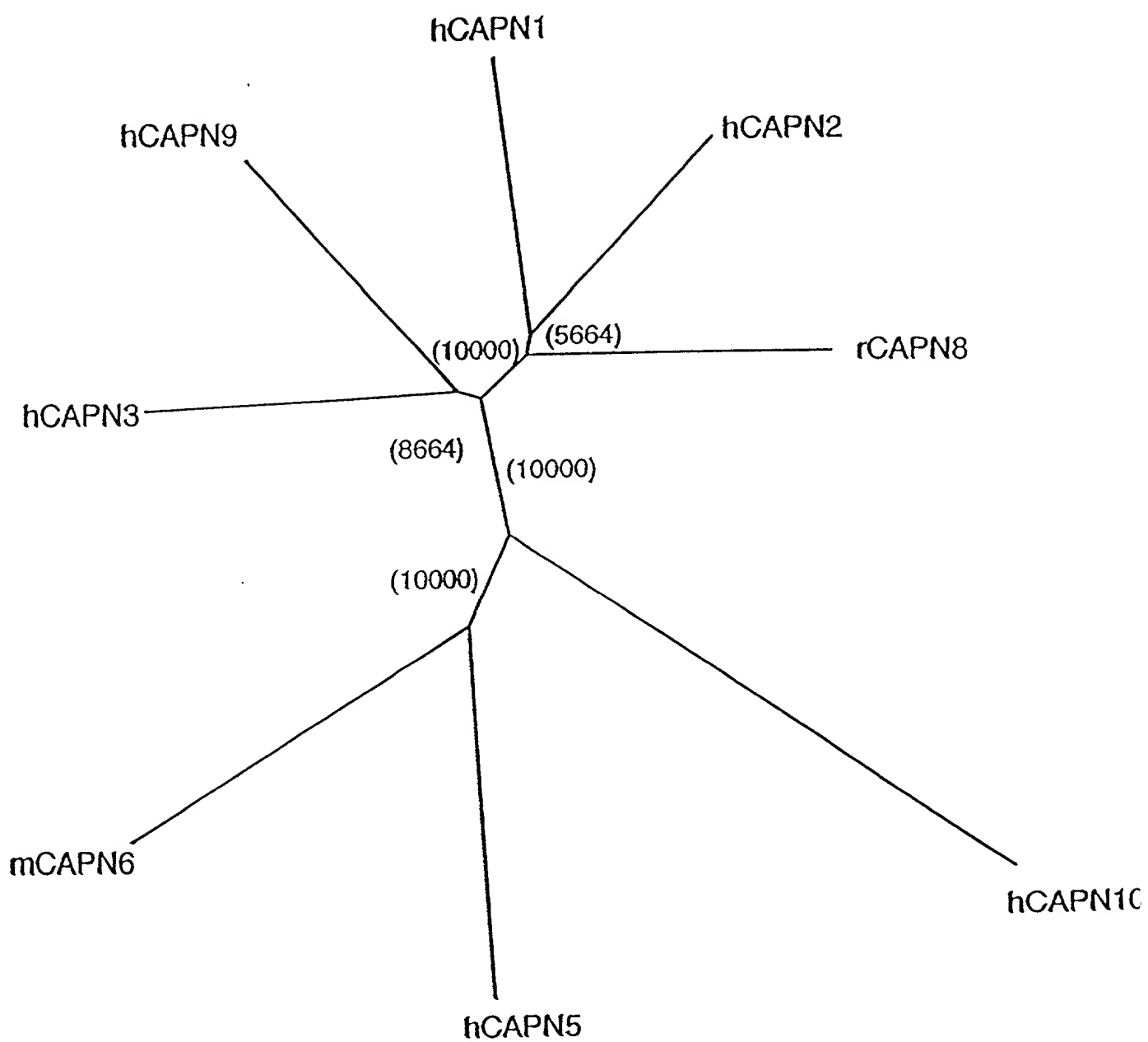


FIG. 6

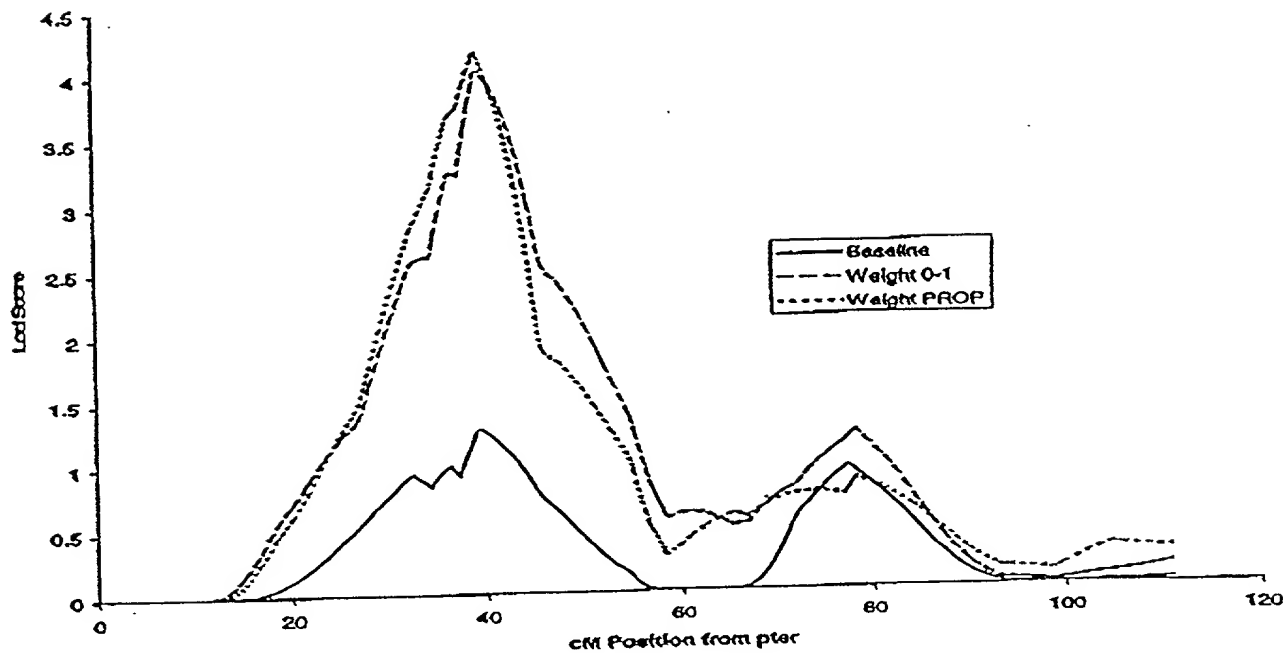


FIG. 7A

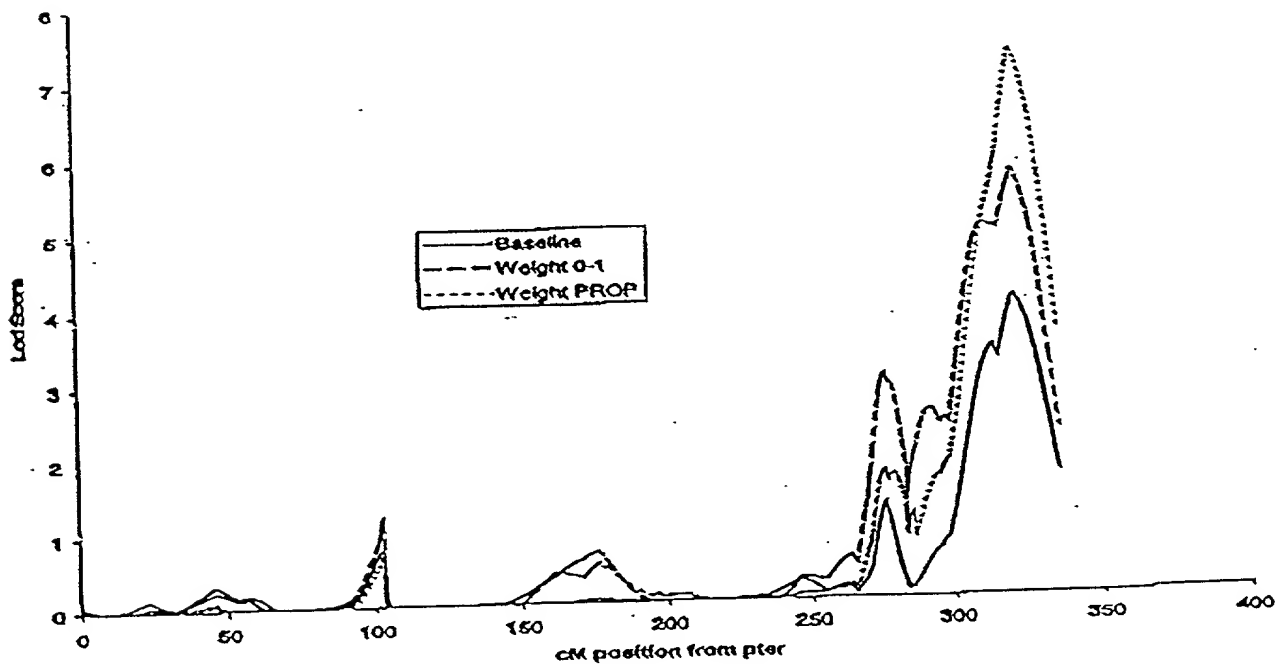


FIG. 7B

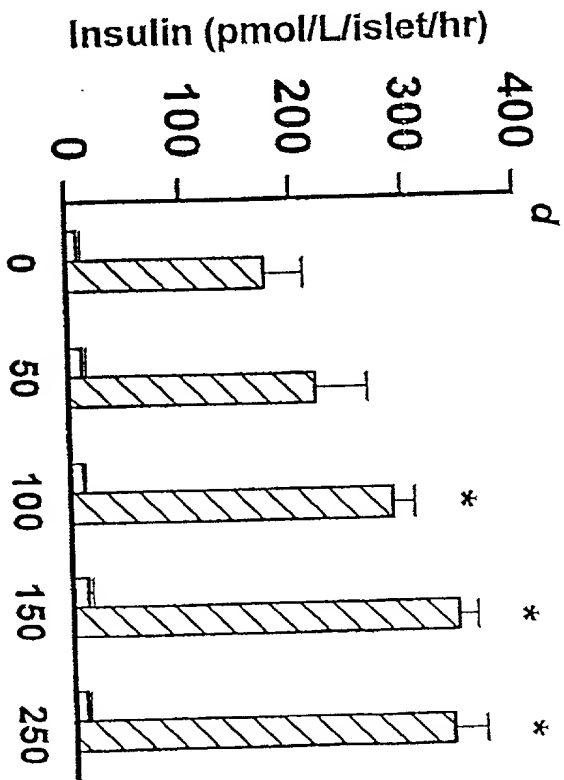
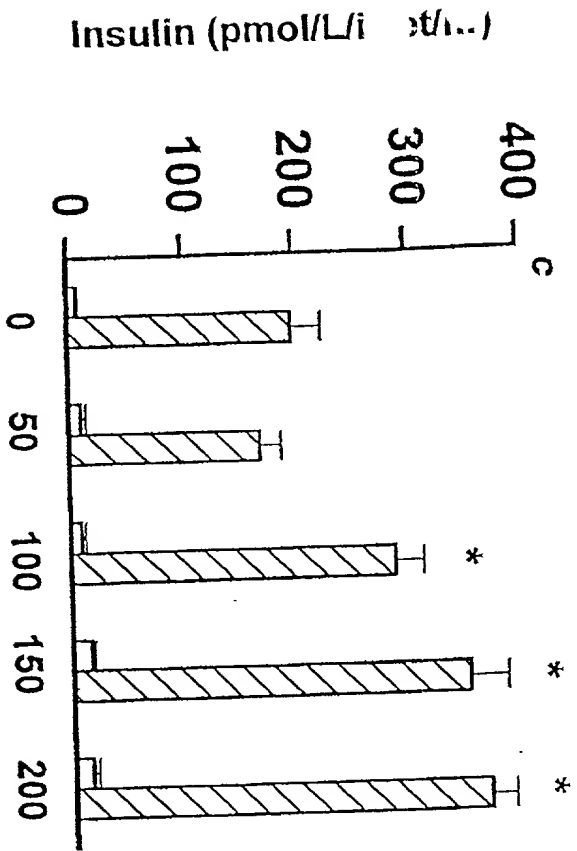
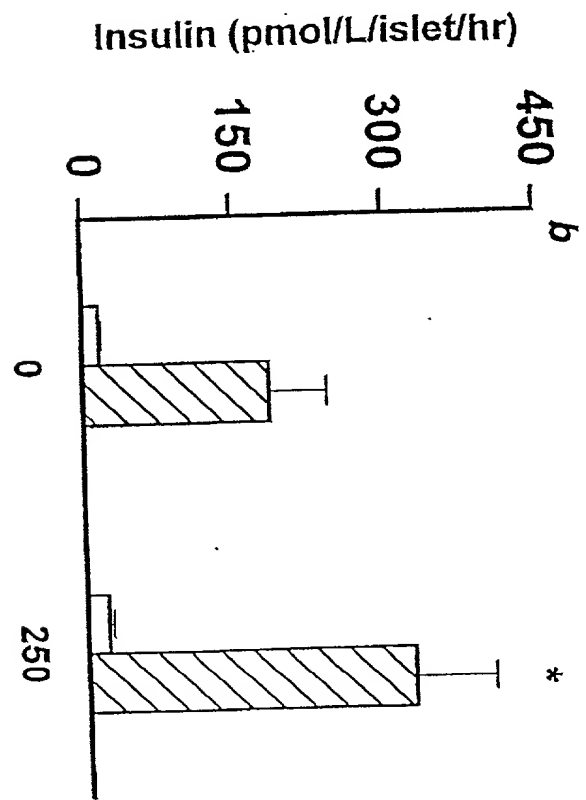
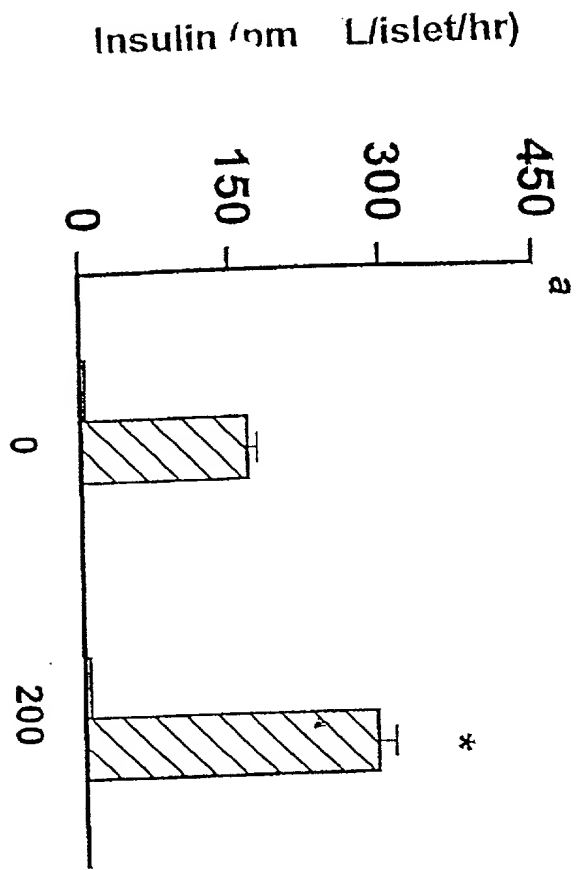


FIG. 8

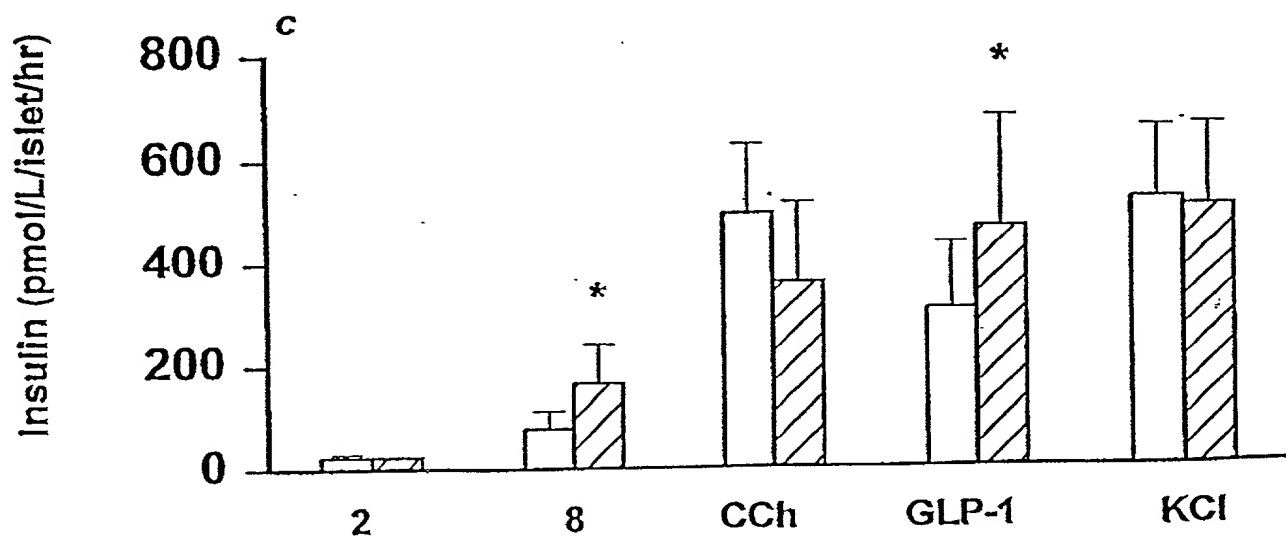
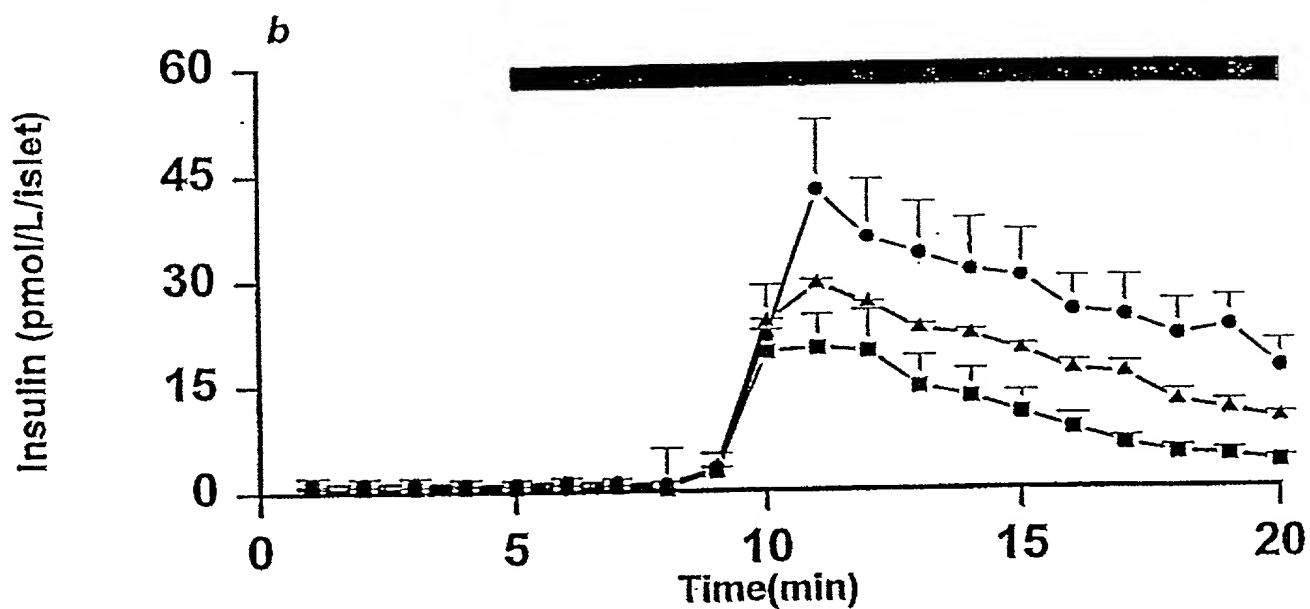
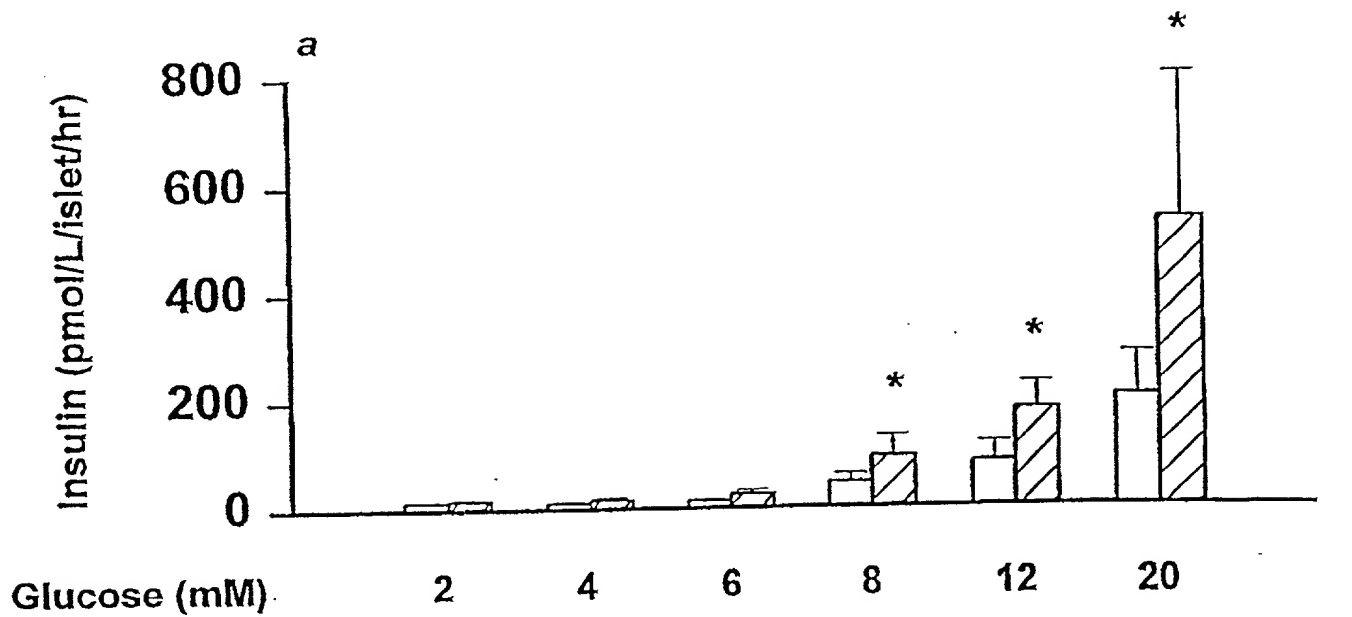


FIG. 9

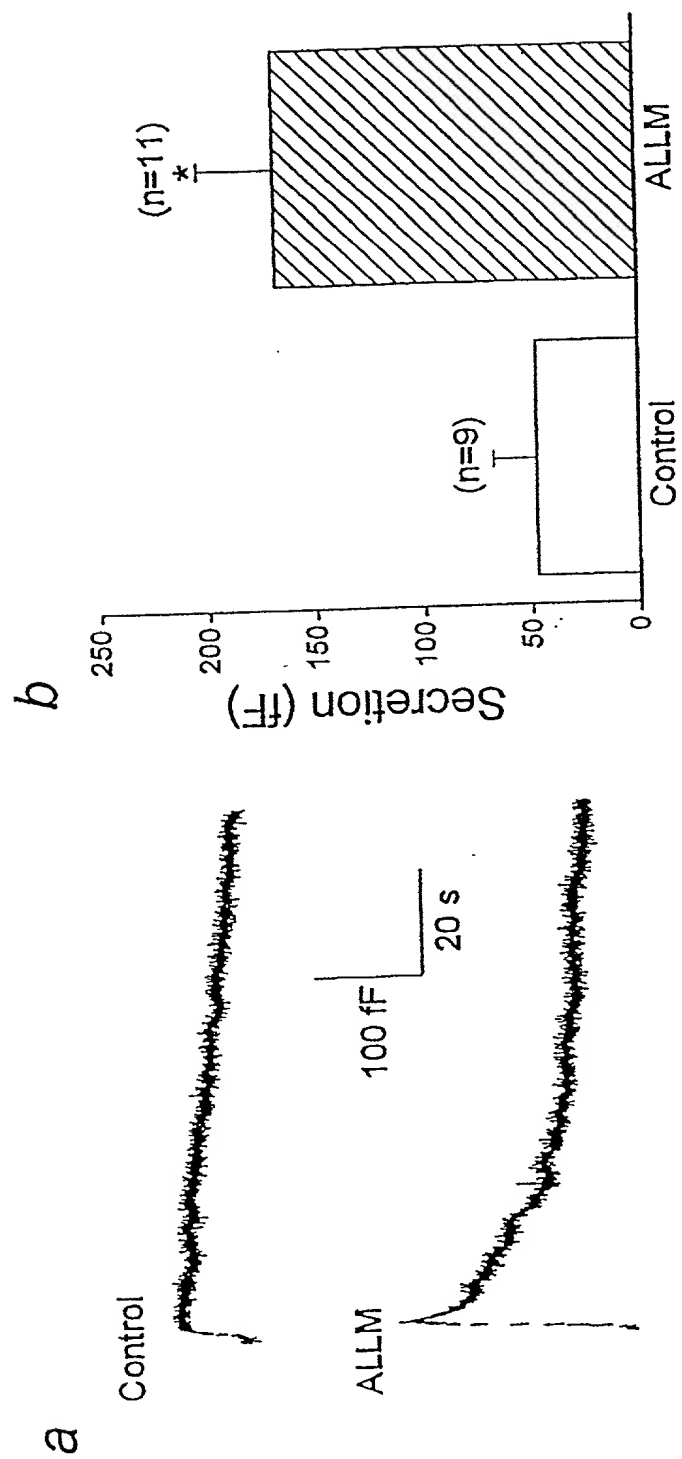


FIG. 10

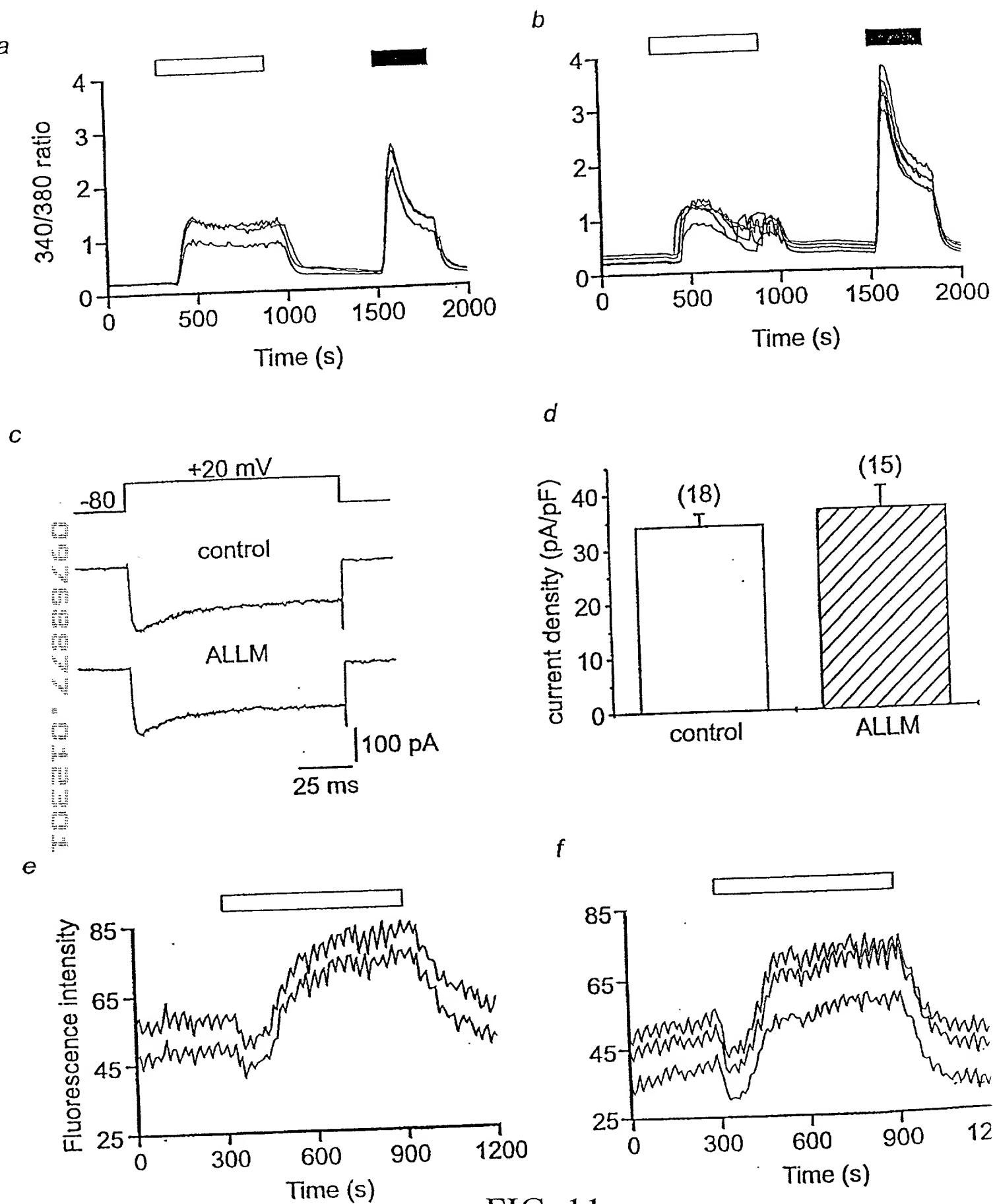


FIG. 11

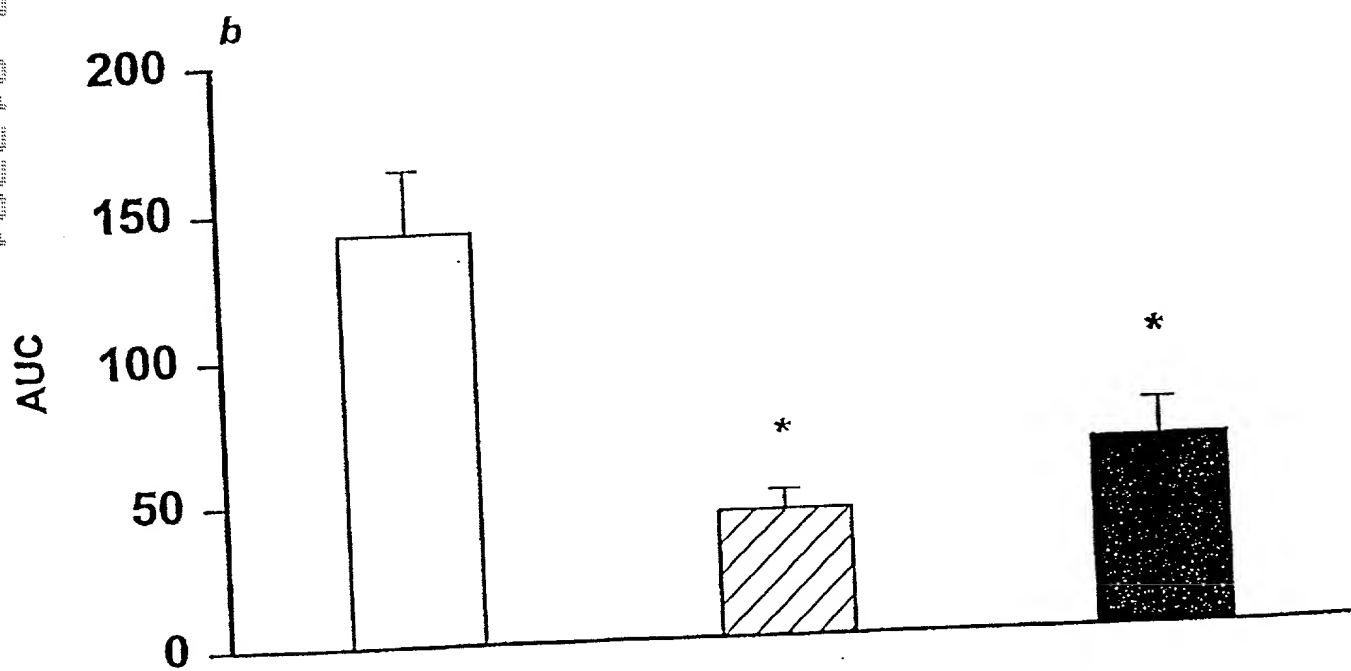
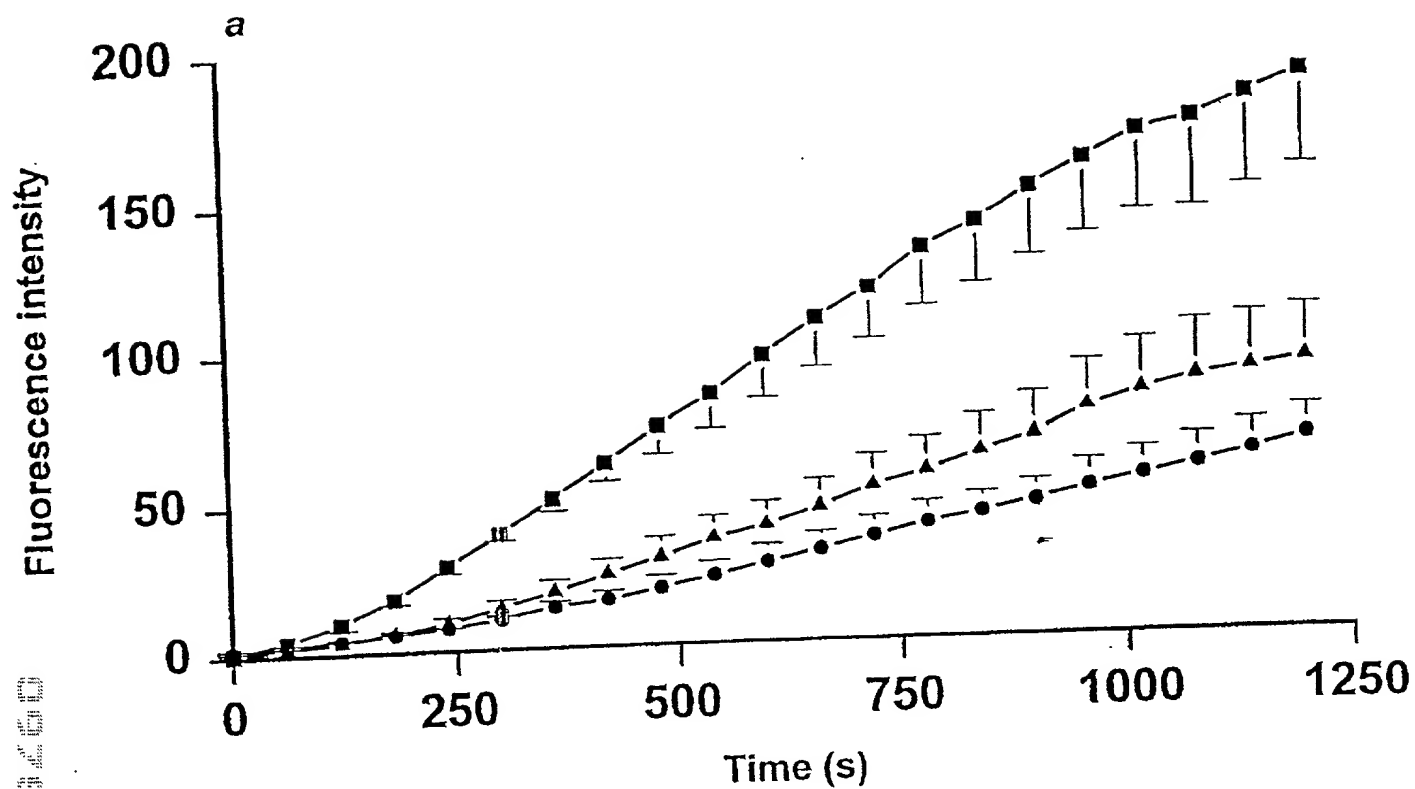


FIG. 12

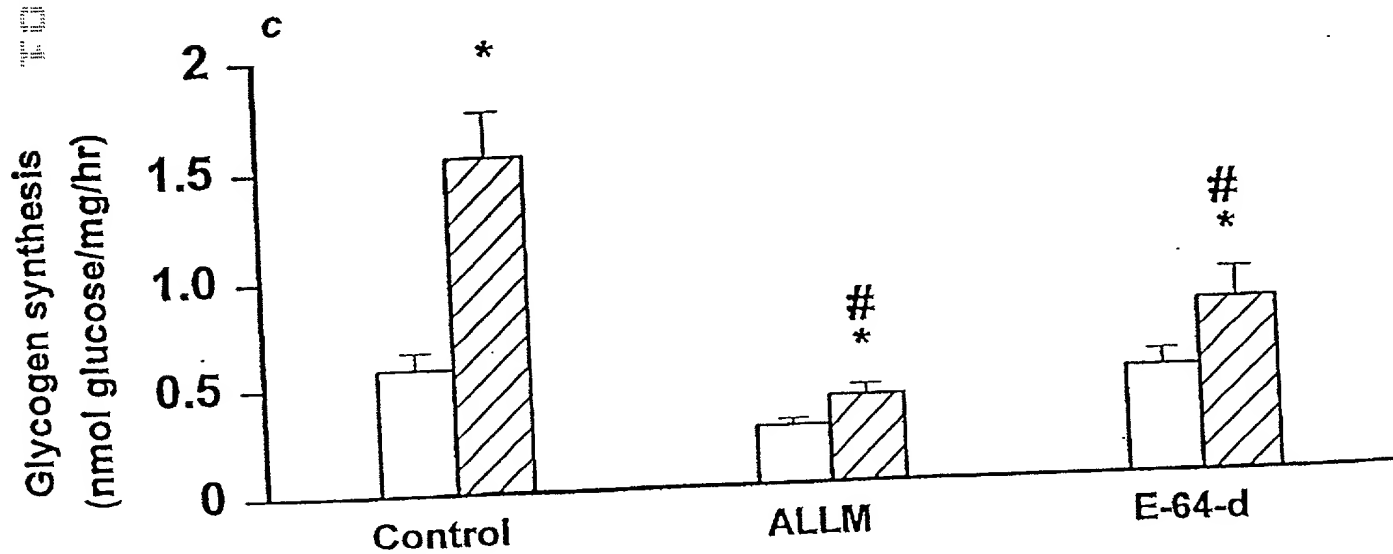
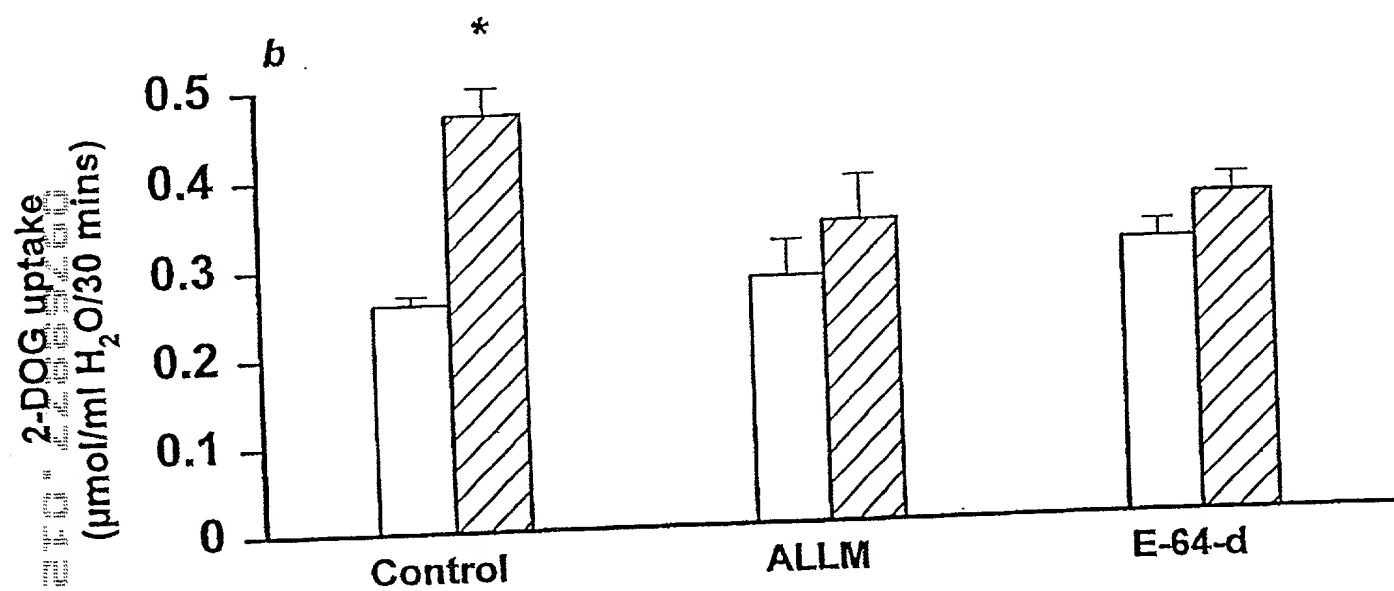
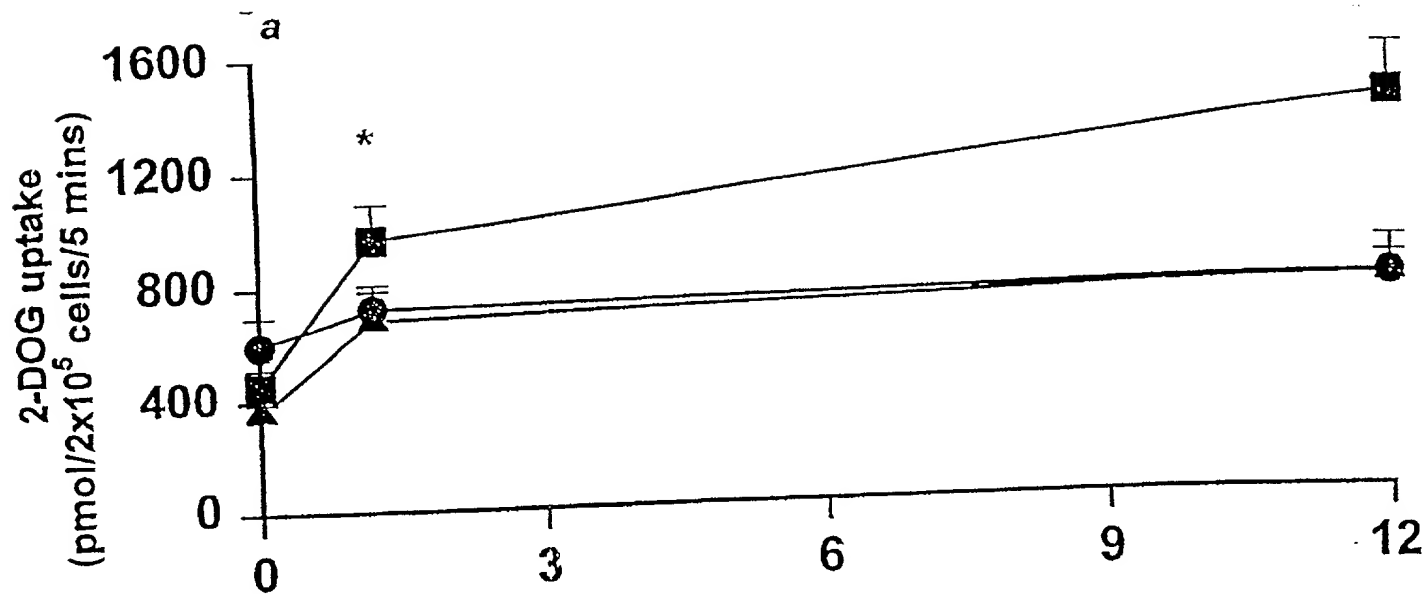


FIG. 13

Fig14. Effect of 48 hours exposure of islets to calpain inhibitors on insulin secretion

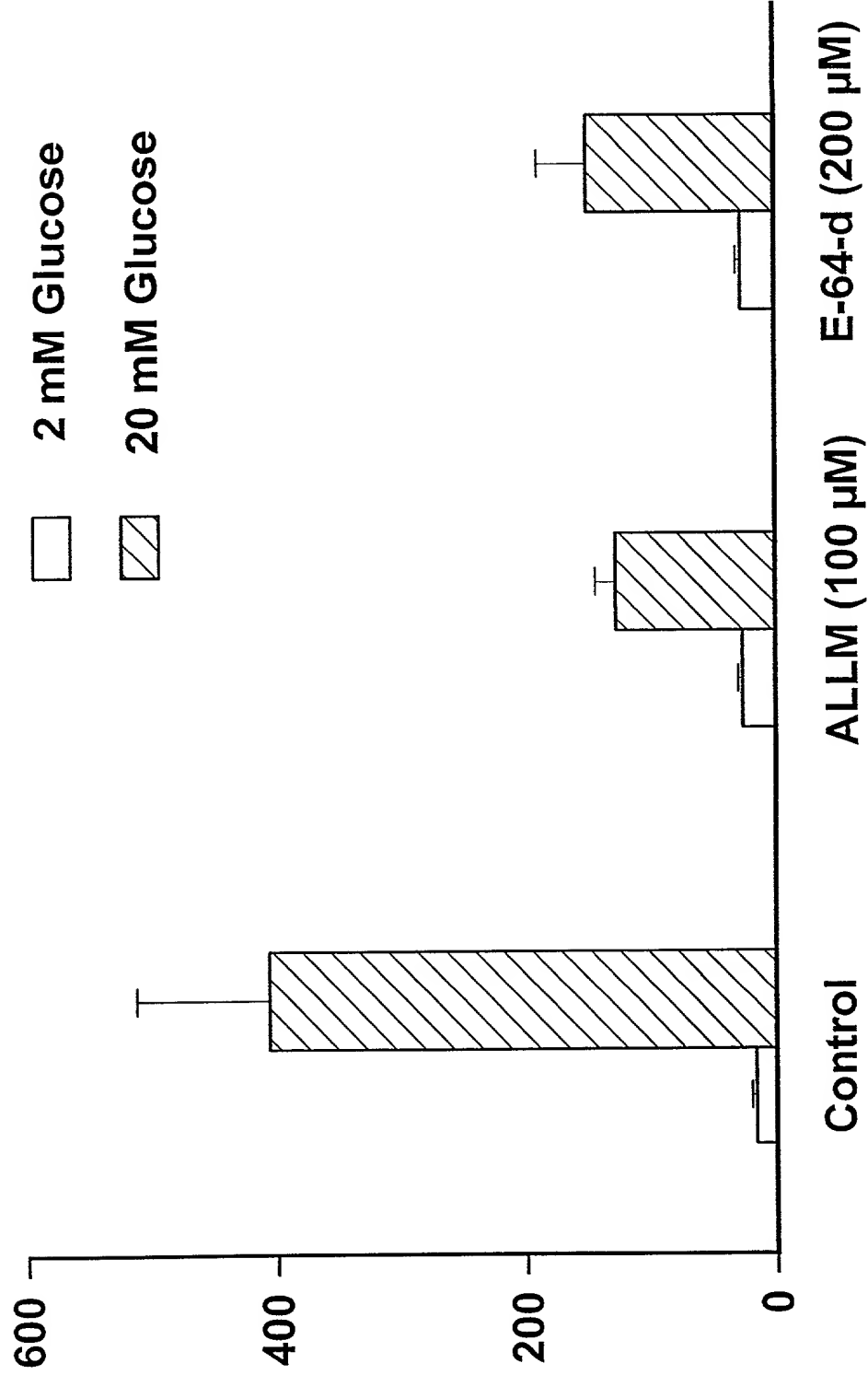


Fig 15 Insulin content in 48 hour cultured islets (n=4)

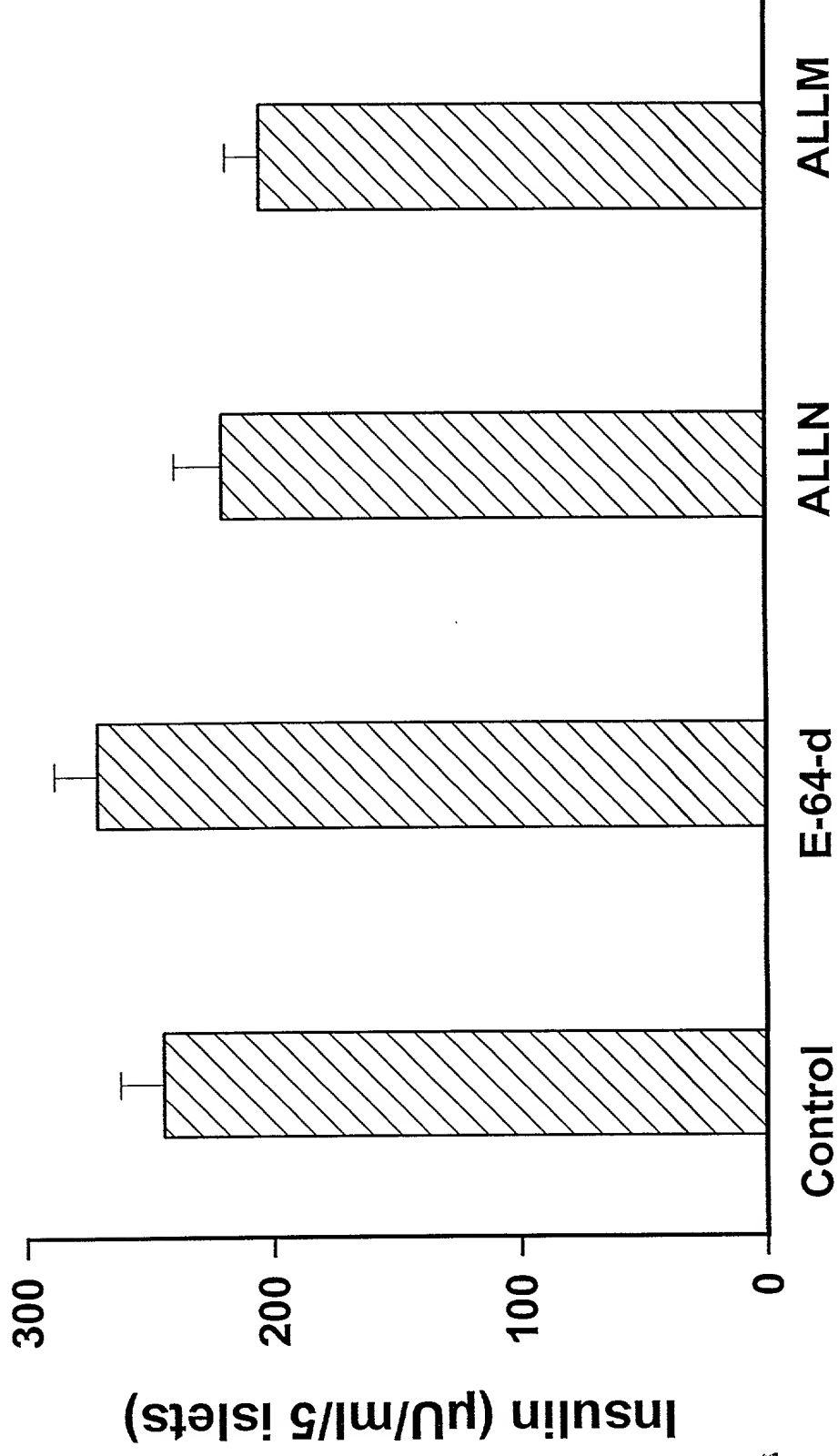


Fig16. ALLM dose response in 48 hour treated islets

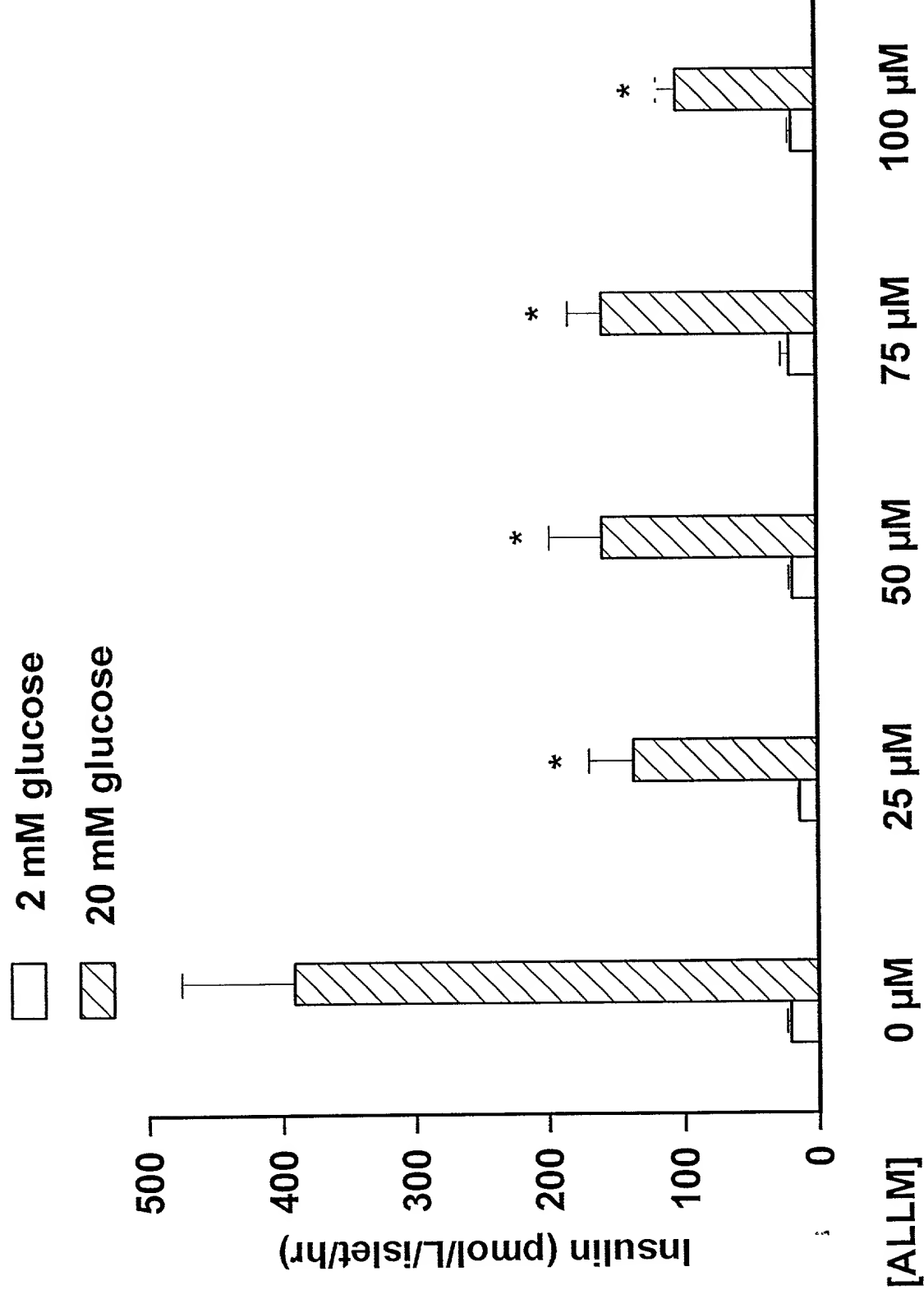
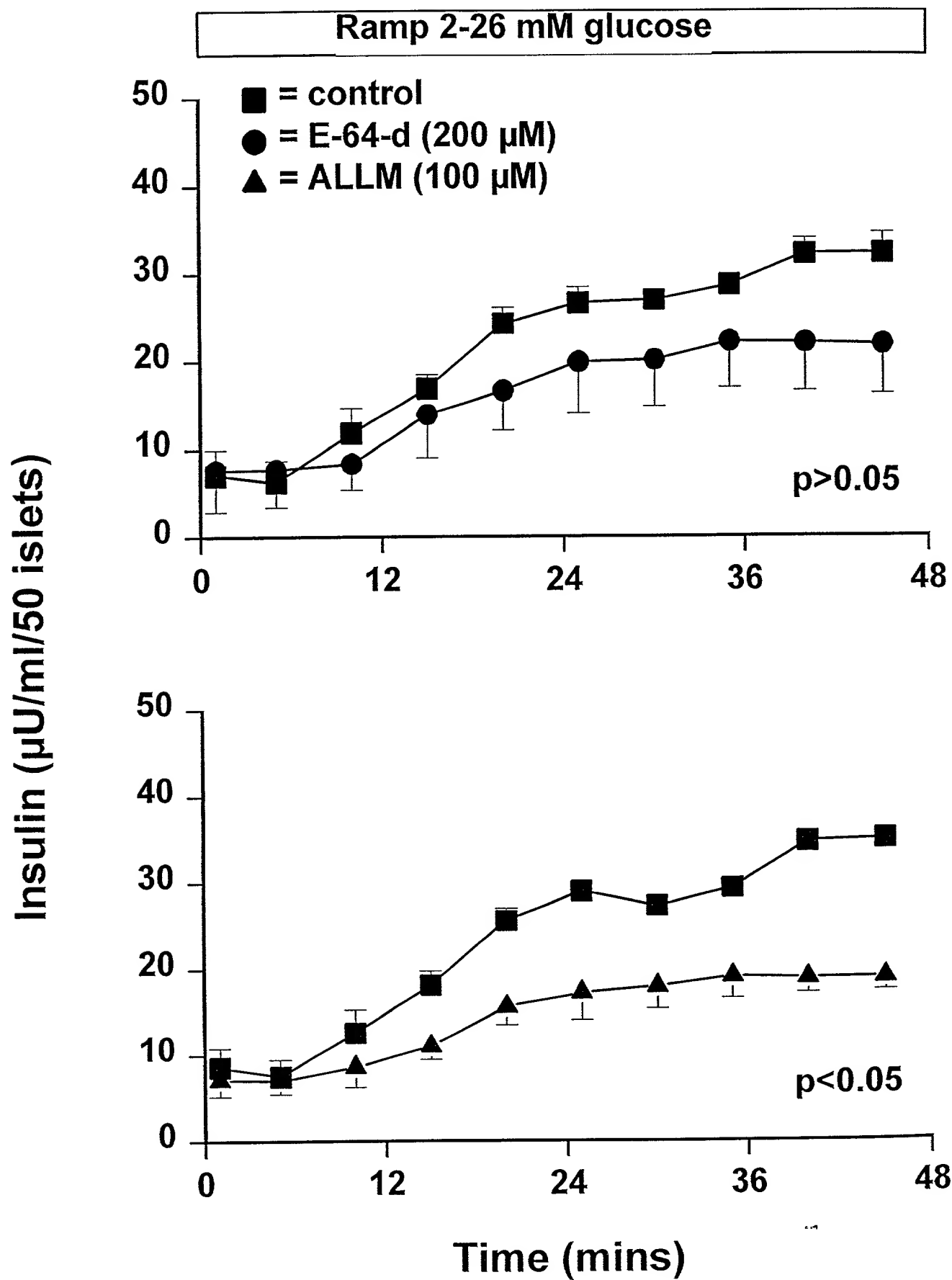


Fig17. Perifusion of 48 hour cultured islets (n=4)



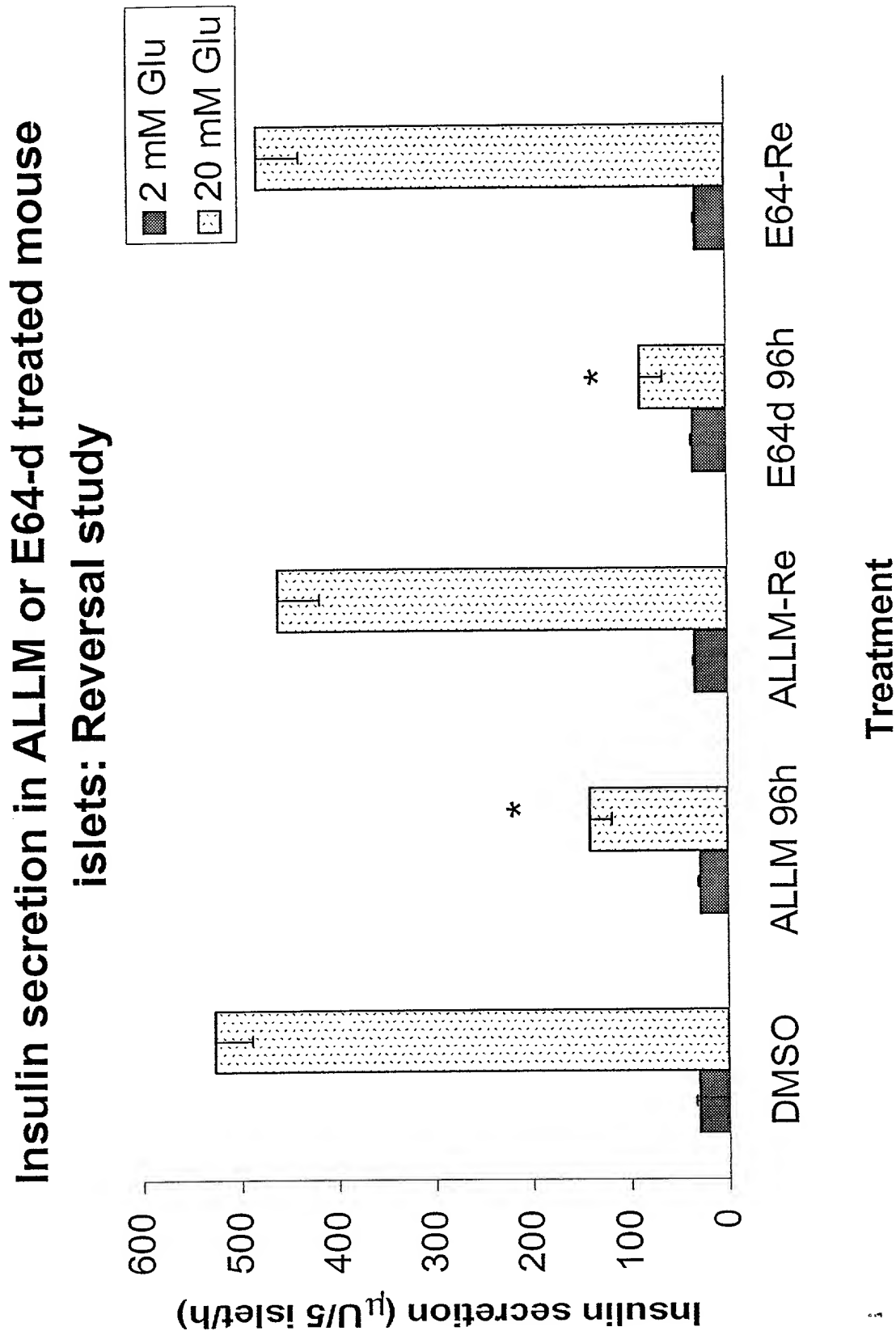
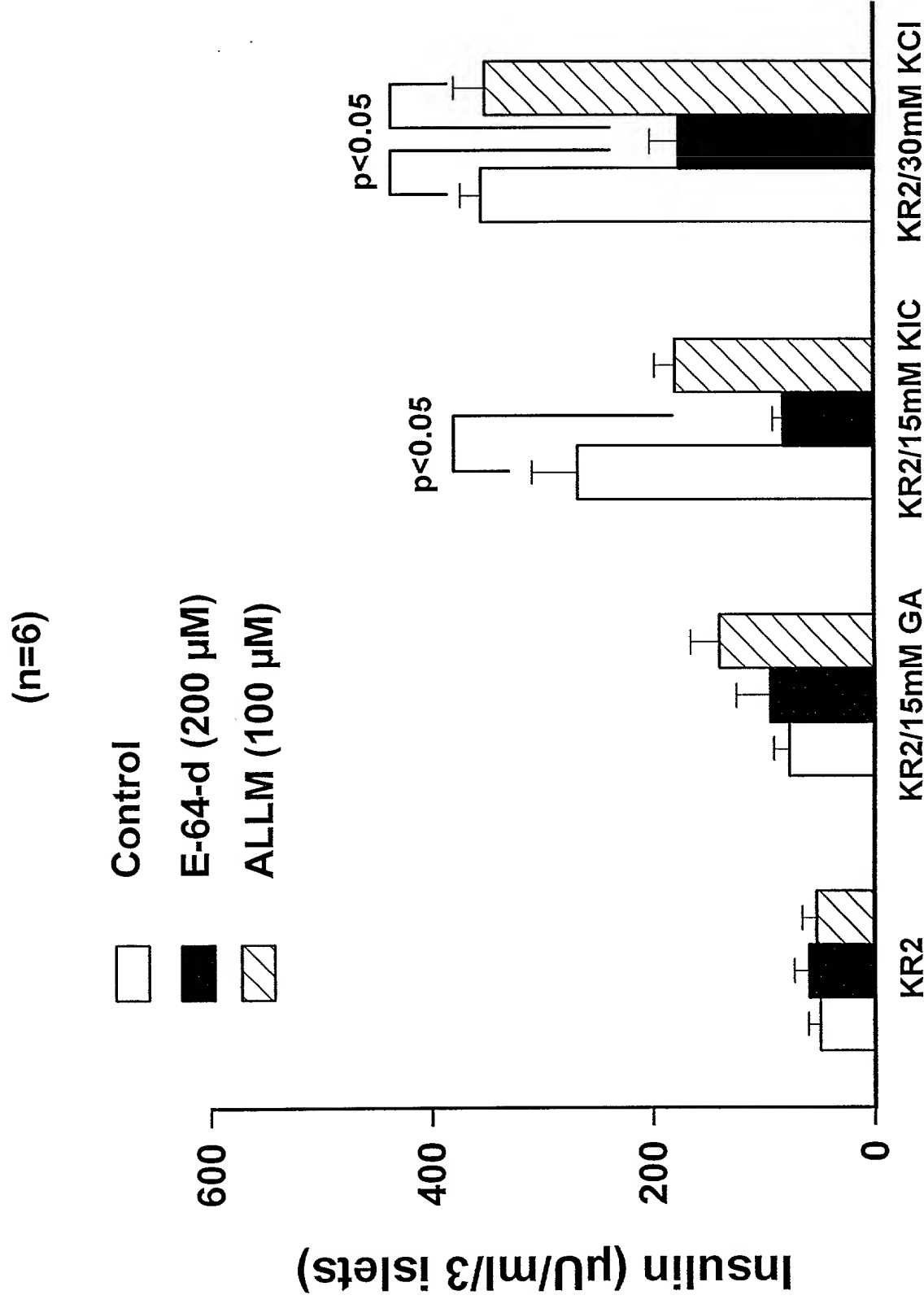


Fig. 18

Fig19. Insulin secretion by islets following exposure to calpain inhibitors for 48 hrs



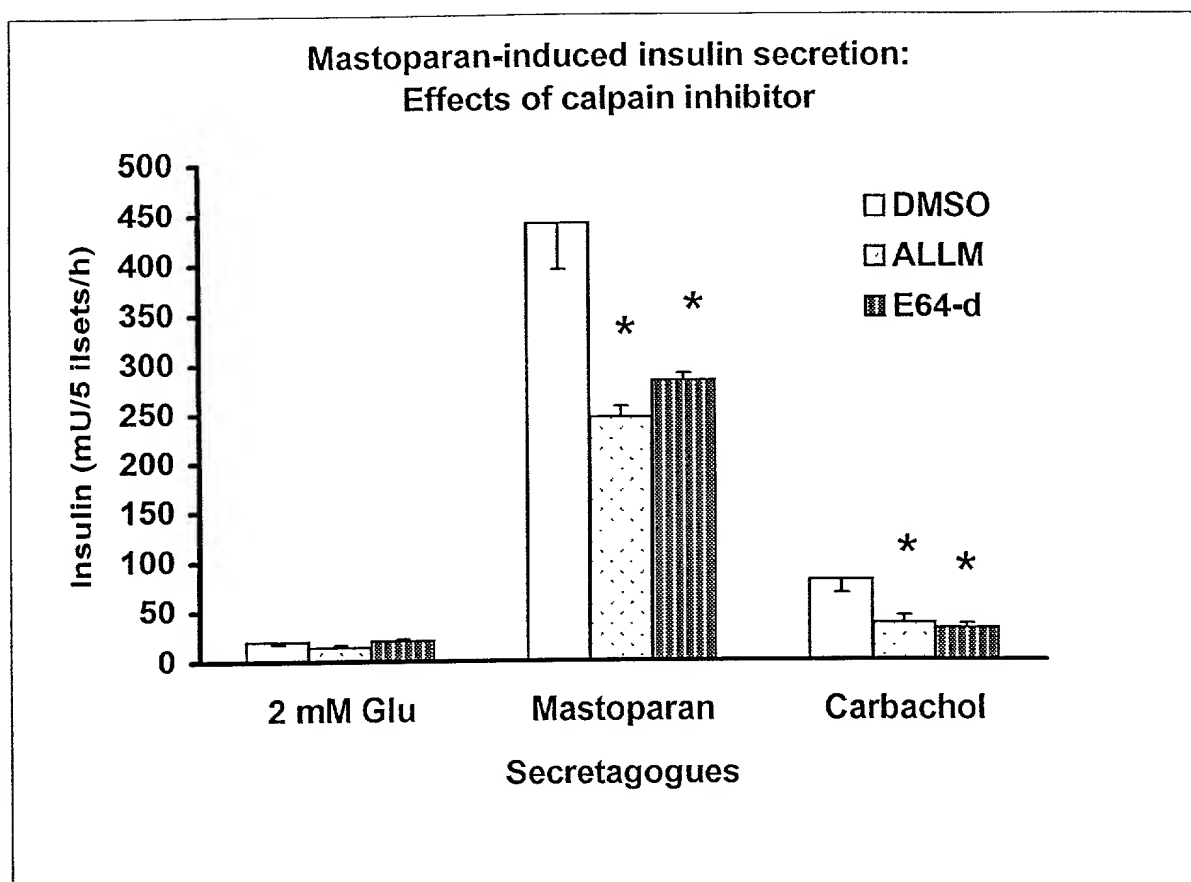
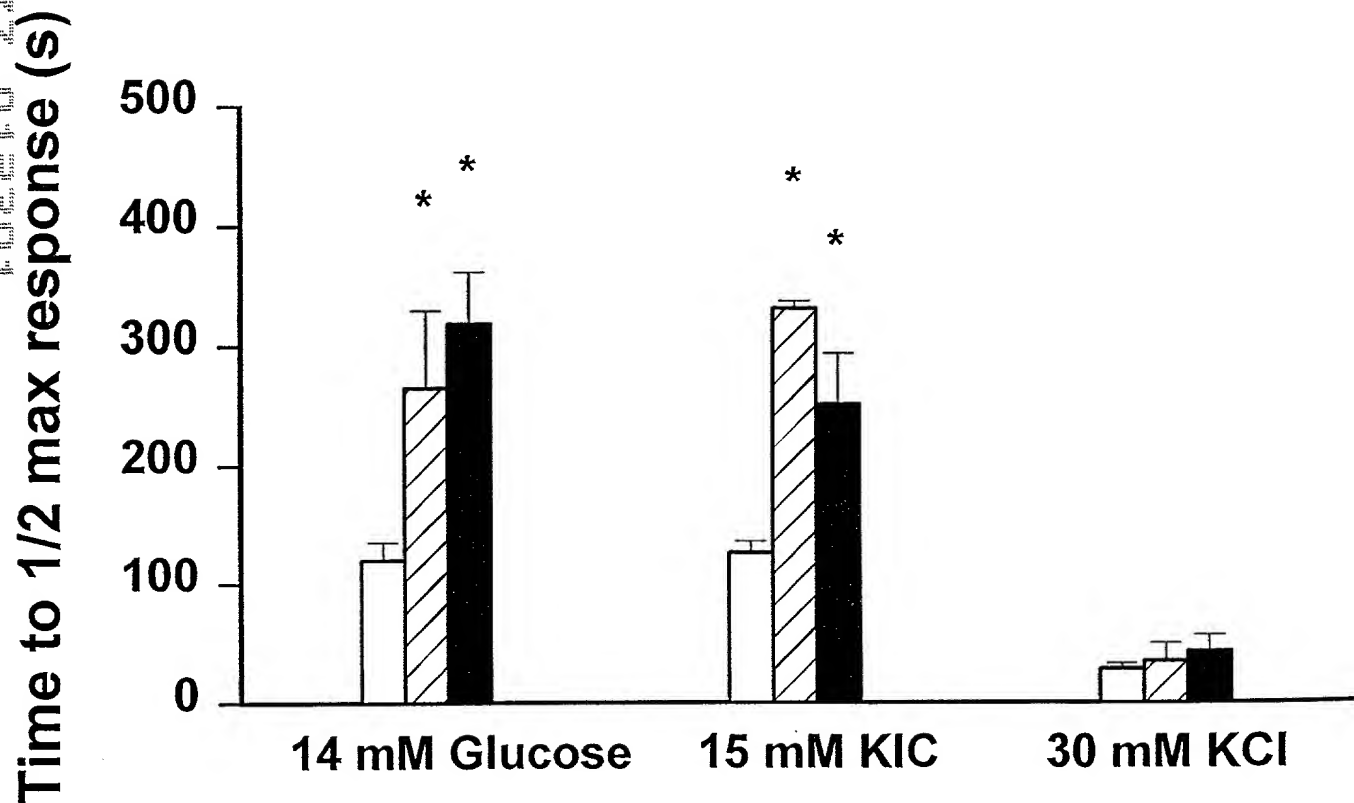
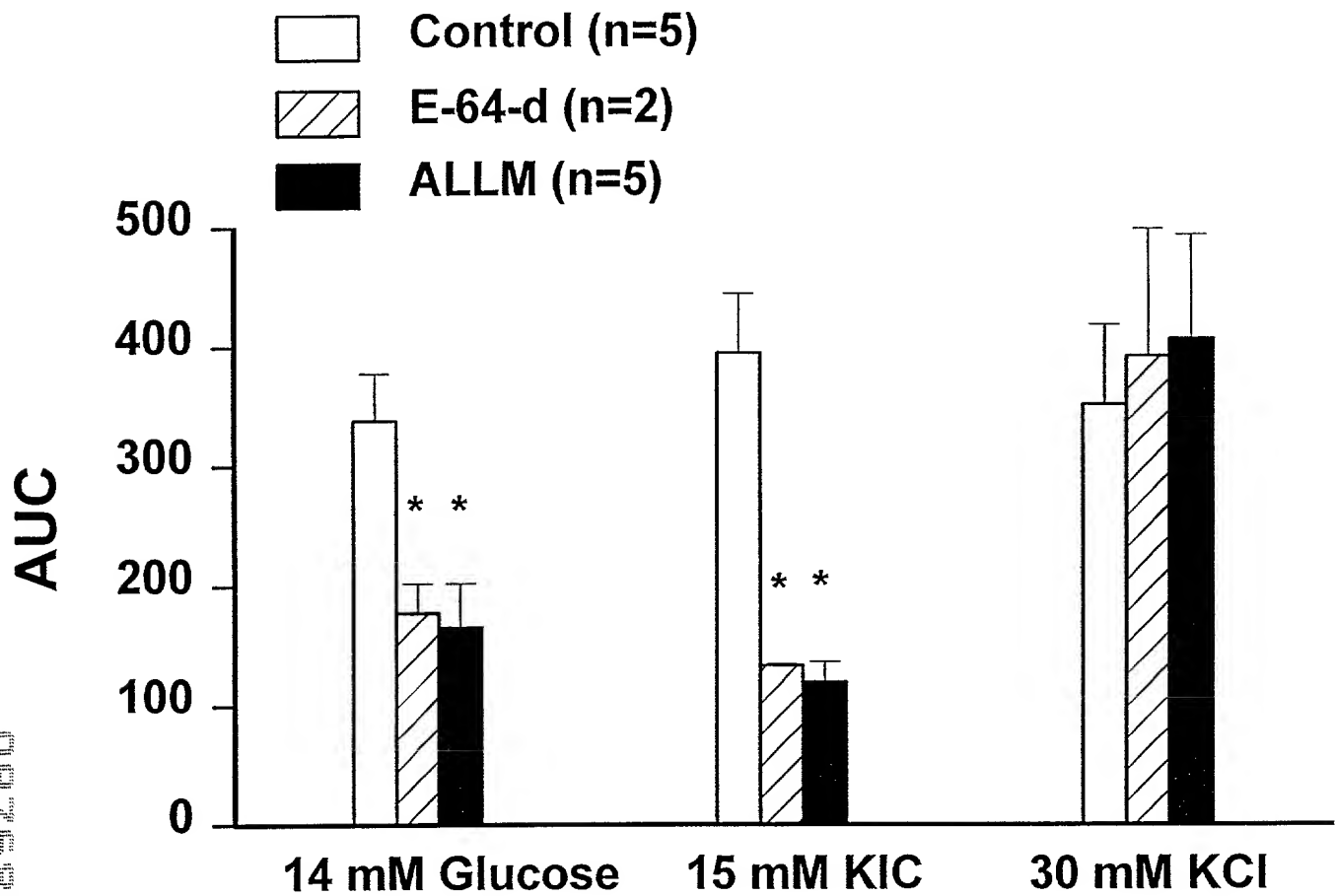


FIG. 20

Fig 21. $[C^{2+}]_i$ responses to glucose, KIC and KCl



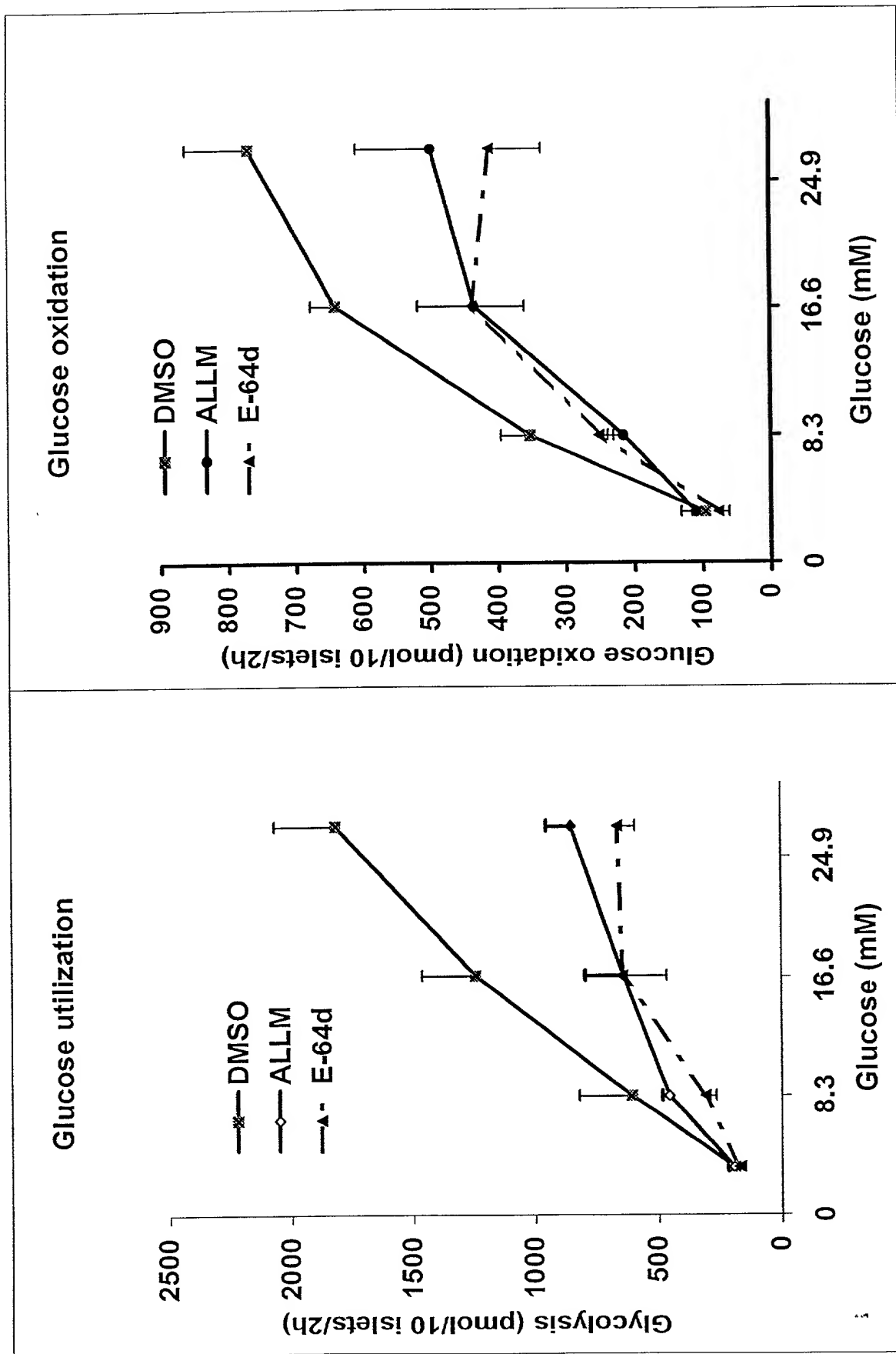
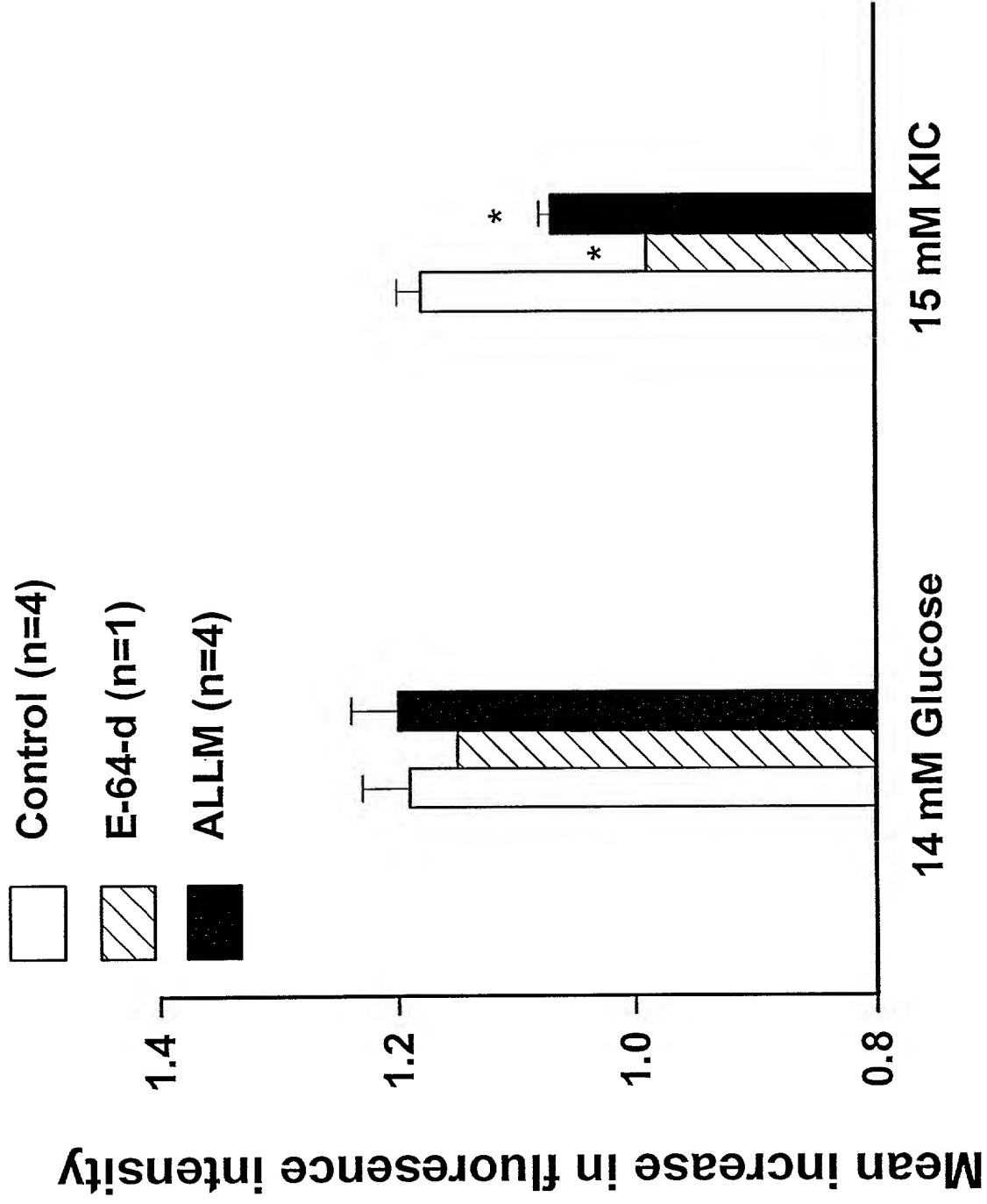


Fig. 22

Fig 23. NAD(P)H responses to glucose and KIC



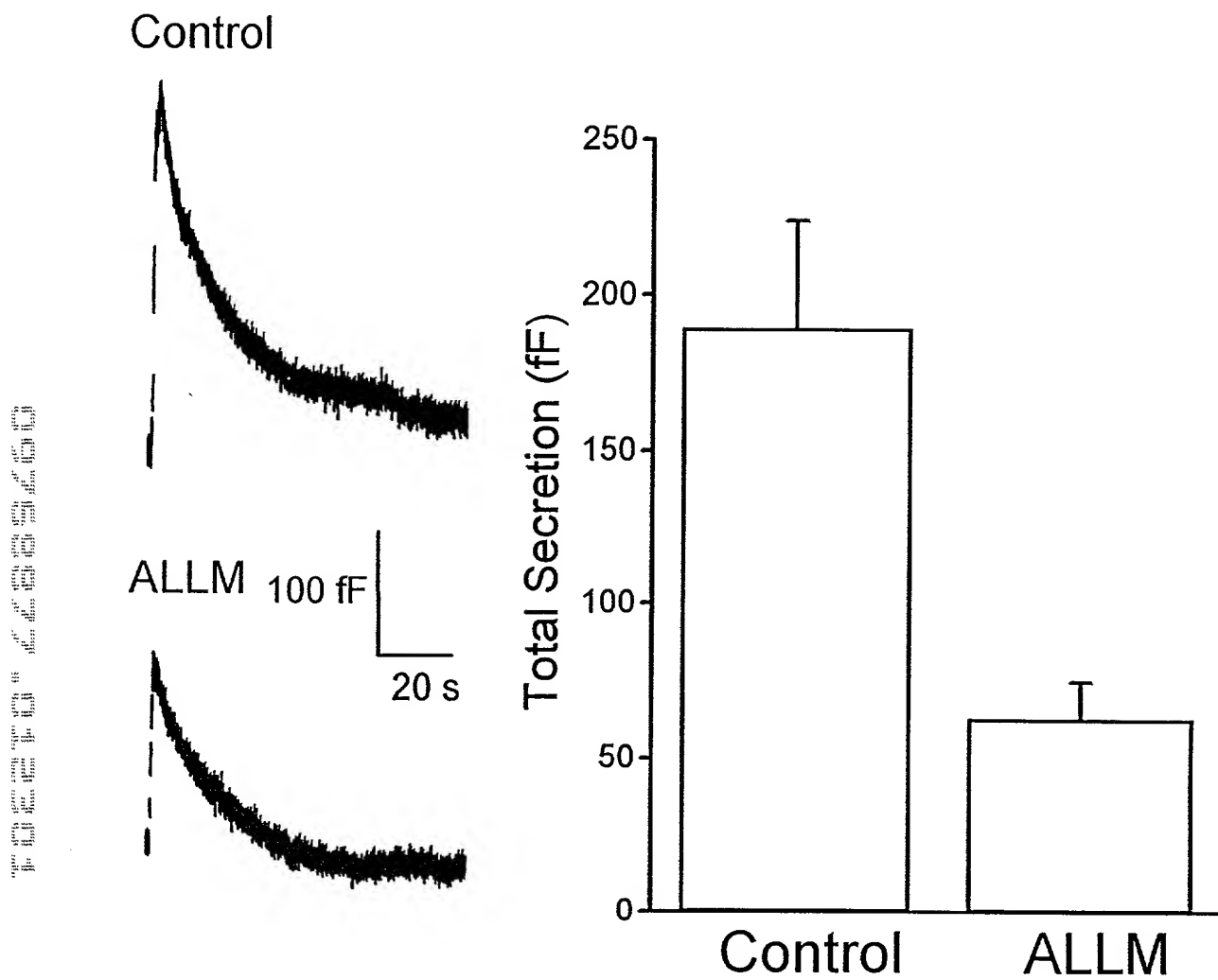


Fig. 24. Measurement of membrane capacitance in isolated β -cells

A black and white photograph showing a dense, dark forest. Numerous bright, white, star-shaped flowers are scattered throughout the foliage, creating a high-contrast, speckled effect against the dark background. The flowers appear to be small and delicate, possibly wildflowers or small blossoms. The overall texture is very busy and detailed due to the high contrast and the density of the plants.

[illegible]

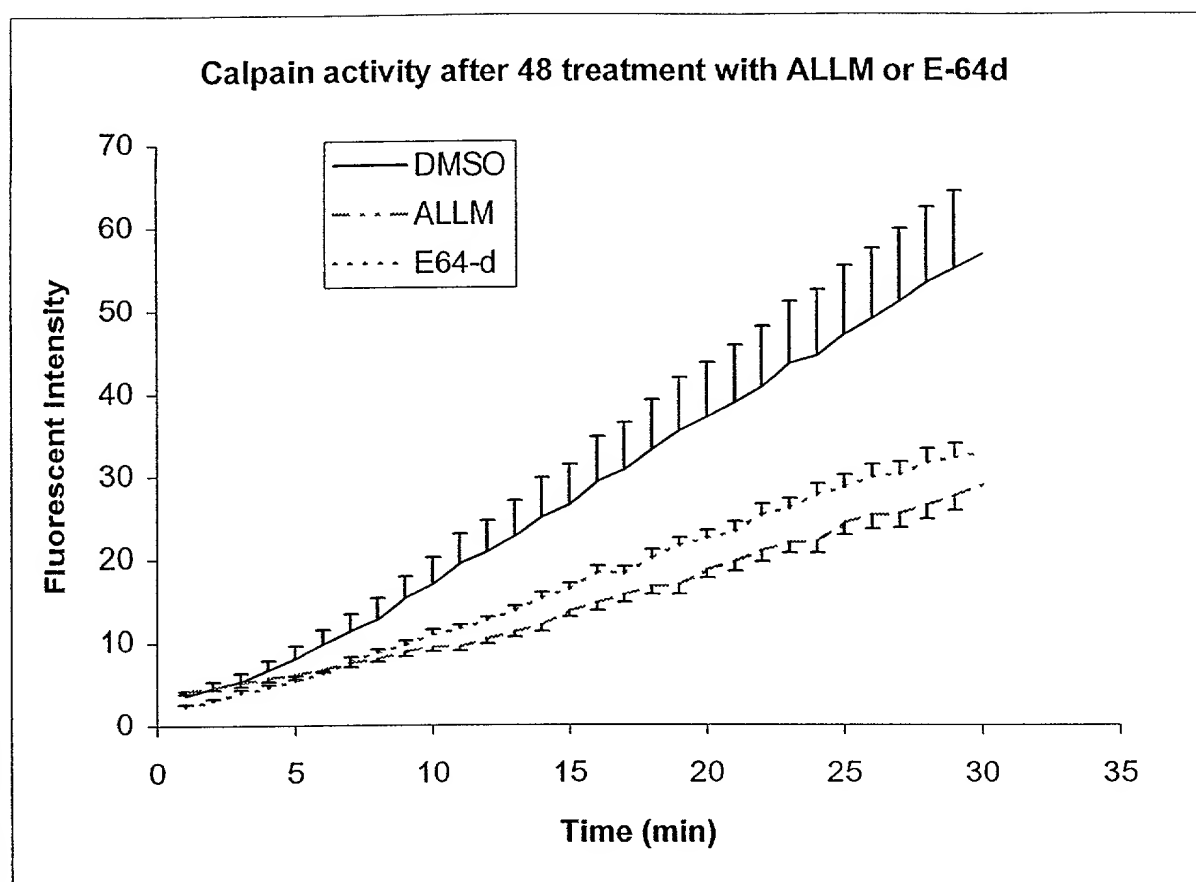


FIG. 26